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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Mid-Atlantic Region

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (201) 331-2909

July 28, 1997

WARNING LETTER

Mr. William Fletcher
Chief Executive Officer
Teva Pharmaceuticals USA
650 Cathill Road
Sellersville, Pennsylvania 18960

File No. 97-NWJ-43

Dear Mr. Fletcher:

During an inspection of your manufacturing facility located at 209 Mclean Boulevard, Paterson, New Jersey 07504, from June 9 - 23, 1997, an Investigator from this office reviewed the qualification of a foreign supplier for Clindamycin Hydrochloride 150 mg Capsules. This inspection resulted in documented deviations from Current Good Manufacturing Practice Regulations (cGMPs), Title 21, Code of Federal Regulations (CFR), Parts 210 & 211. These deviations, were noted on the Form FDA483, List of Inspectional Observations, issued to you at the close of the inspection.

The above stated inspection revealed that Clindamycin Hydrochloride 150 mg Capsules manufactured at your Paterson facility are considered to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the ACT), in that the methods used in, or the facilities and/or controls used in manufacturing are not in conformance with cGMPS, as follows:

1) Currently marketed lots of Clindamycin HCL 150 mg Capsules were released with insufficient stability data to support the expiry date. The only stability data available is from lot 20281, which failed impurity specifications at the 18 month station.

2) Your firm did not evaluate all impurities prior to releasing marketed lots. A stability indicating method to detect all impurities in the Clindamycin drug substance, has not been developed for the current supplier.

3) The Process Validation was inadequate, in that data was selectively chosen from five different lots manufactured from 1993-1997, rather than three

RELEASE

REVIEWED BY [signature] 7/25/97
C.O. DATE

consecutively manufactured lots. In addition, data to support blend uniformity was taken from Lot 20281, which ultimately failed impurity specs.

4) In determining the qualification of the foreign drug supplier, the drug substance differed significantly in particle size and bulk density specs from the previously approved supplier, yet this material was approved and used in released lots.

5) The "Procedure for Selecting, Sampling, Tracking and Testing of Stability Samples" allows drug substance storage for up to one month for antibiotic mix and three months for a granulation, however there was no data to support these hold times.

6) Your firm failed to document laboratory investigations in which alert limits for accelerated stability were exceeded for Lot 20281. Additionally, there was no documentation that retesting of voided samples for this lot was taken from the same composite sample.

7) Procedures are not adequately followed, for example:

a) Stability samples for Lots 28125 and 28126 were not placed on stability until 31 days after being manufactured. Procedures allow for [redacted] days placement.

b) Batch records for Lots 28048, 28125, and 28126 failed to identify these as stability samples. Procedures specify that stability samples are identified on batch records.

The above list is not intended to be all-inclusive of deficiencies at your facility. It is your responsibility to ensure that the drug products you manufacture are in compliance with the Act and the regulations promulgated under it. Federal agencies are routinely advised of Warning Letters issued so that they may take this information into account when considering the award of contracts.

We are in receipt of your written response, dated July 2, 1997, to the FDA483 List of Inspectional Observations. Your commitment to

recall all distributed lots of Clindamycin HCL 150 mg Capsules, is acknowledged with this letter. We also note that during the inspection, current production and distribution of this product was suspended. While we find your actions satisfy our immediate concerns, we encourage you to review other products that may have similar deficiencies with respect to validation and foreign supplier qualification.

When validation issues have been resolved with respect to this product, a reinspection will be necessary to verify corrective actions taken.

We recognize that your firm is in the process of revising procedures and implementing organizational changes in order to improve the overall Quality Assurance Systems at each manufacturing facility. We look forward to our meeting, scheduled for August 5, 1997 to discuss these plans and the status of products covered under the consent decree.

You should notify this office in writing of any additional steps your firm has implemented with regard to this product and a review of approved products which may have similar deficiencies, within 15 days of receipt of this letter. If additional time is needed to comply with this request, please provide a written statement indicating the timeframe within which this information can be provided. Your reply should be sent to the New Jersey District Office, FDA, 10 Waterview Blvd., 3rd Floor, Parsippany, New Jersey 07054, Attention: Mercedes B. Mota, Compliance Officer.

Sincerely,

Douglas Ellsworth

Douglas Ellsworth
District Director
New Jersey District

**CERTIFIED MAIL -
RETURN RECEIPT REQUESTED**

MBM:np